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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STANDLEY, STEVEN H	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
09/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/734,731	WEIHE ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-12,14,15 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-12, 14-15,and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendment filed 5/29/07 has been made of record. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Objections/Rejections: Withdrawn

Claim Rejections - 35 USC § 112

2. Rejection of claims 1-4, 7-12, and 14-15 under 35 USC § 112, 1st paragraph is withdrawn because Applicant deleted "...a protein encoded by a nucleic acid which is the reverse complement of a polynucleotide."

3. Rejection of claims 1-4, 7-12, and 14-15 under 35 USC § 112, 1st paragraph is withdrawn because Applicant deleted "...ionic milieu."

4. Rejection of claims 1-4, 7-12, and 14-15 under 35 USC § 112, 2nd paragraph is withdrawn because applicant changed "pain-regulating" to "a candidate."

5. Rejection of claims 1-4, 7-12, and 14-15 under 35 USC § 112, 2nd paragraph, as being indefinite and unclear because the relationship between steps a and b are unclear is withdrawn due to applicant's amendments.

6. Rejection of claims 1-4, 7-12, and 14-15 under 35 USC § 112, 2nd paragraph is withdrawn also because Applicant deleted "ionic milieu."

4. Rejection of claims 1-4, 7-12, and 14-15 under 35 USC § 112, 2nd paragraph is withdrawn because applicant has amended claim 1 to read 'candidate' and therefore the scope of step c may include the determination of step b, or a further step of testing in an animal.

Objections/Rejections: Maintained/New Grounds

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Rejection of claims 1-4, 7-12, and 14-15 and 33 under 35 USC § 112, 1st paragraph, enablement is maintained for the reasons made of record in the office action dated 6/14/05, 3/09/06, and 11/29/06 and the reasons below. Applicant is enabled for a method of identifying substances that bind to full-length Vglut1, and then testing those substances in an animal model of pain, however applicant is not enabled for proteins 90% homologous or peptides more than 10 amino acids long. Further, applicant is not enabled for a method wherein measuring a "functional parameter modified by the

binding of a test substance...wherein measuring said functional parameter involves measuring the regulation, inhibition or activation of [generic] receptors, [generic] ion channels or [generic], or via a measurement of modification of [generic] gene expression, [generic] pH or membrane potential or via [generic] modification of enzyme activity or [generic] concentration of second messenger. " The scope of the peptides included is 90% of any 10-mer of vGlut1, which is reasonably an enormous number of polypeptides that have no structural or functional relationship to the full-sized molecule. The scope of the 'measurements' is so broad as to be readable upon unknown and undiscovered ion channels, receptors, or enzymes, as well as unknown and undiscovered relationships between vglut1 and any known or unknown ion channels, receptors, or enzymes. Furthermore, the scope of measuring "membrane potential" in response to contacting vglut1 with a candidate molecule is so broad as to measure membrane potentials that have unknown and undisclosed relationships with the contacting of vglut1 with a candidate compound. In other words, the recitation is so broad as to only require incubating a test substance with something that has vglut1 in it, which could be a cell or anything else. For fur

Applicant argues that claim 1, after amendment, does not require that the method identify a pain regulating substance. The examiner agrees.

Applicant argues that a person of skill can readily envision protein or polynucleotide which is 90% homologous to vglut1. This is not found persuasive because one skilled in the art, having performed the recited assay would not know if the compound were in any way relevant to vglut1 or even the peptide or nucleotide

expressed, since it measures things with no known or disclosed relationship to vglut1 or any of its peptides.

Applicant argues that the tests required to measure the listed functional parameters are all within the skill set of one of skill in the art. This is not found persuasive because one skilled in the art does not know how all of the generic measurements recited relate to vglut1.

10. Rejection of claims 1-4, 7-12, and 14-15 and 33 under 35 USC § 112, 1st paragraph, written description is maintained for the reasons made of record in the office action dated 6/14/05 and 3/09/06. Applicant's arguments have been fully considered and not found to be persuasive. Applicant argues on page 7 of Remarks that a person skilled in the art could measure the functional parameters using tests which are generally known to those skilled in the art. This is not found persuasive because, for instance, the art does not teach an enzyme measurement one should take having contacted a compound to the transporter vglut1. The art also does not teach an ion channel one should measure after having contacted vglut1 with a compound, and so on. None of these things are taught in the art or the specification.

Further, applicant is claiming identifying compounds that bind to any polypeptide of 10 or more amino acids of that of SEQ ID NO: 4. However, applicant does not have written description of such variants as they relate to finding compounds that modulate vglute. The claims are drawn part polypeptides 10 or more amino acids in length of the polypeptides. The claims do not require that the polypeptides possess any particular

biological activity except binding to a generic substance, nor any particular conserved structure, or other disclosed distinguishing feature. Therefore, there are no clear structural limitations on the complex of polypeptides claimed. Thus, the claims are drawn to a genus of polypeptides that constitute a complex that is defined only by 10 or more amino acids of the protein.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. In the instant application, no such distinctions have The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until

reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only polypeptides comprising the amino acid sequence set forth in a SEQ ID NO: 4 but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

14. Rejection of Claims 1-4, 7-12, and 14-15 and 33 under USC 112, 2nd paragraph for using the term 'functional parameter,' without adequately defining it is maintained for reasons made of record in the office action of 6/14/05 and 3/09/06 and 11/29/06. It is unclear how measuring inhibition or activation of receptors, etc, is measuring a functional parameter. A parameter is a limit or boundary that can be varied in an experiment, not a dependent variable. However, it is unclear what definition Applicant is giving it because the claim recites things that can be measured or controlled and varied.

It is unclear how measuring pH (which is something the experimenter can control) helps identify a substance that is pain-relevant, while it is clear how measuring, for instance expression of the protein, helps identify a pain –relevant substance. Applicant argues on page 9 of Remarks (5/29/07) that if there is an observable change in the "functional parameter" it would indicate the test substance has an effect on it. The examiner respectfully disagrees. A parameter is something one controls to restrict the outcome (dependent variable). One can measure it, but it will not tell you it the substance has an effect on said protein. Please consider revising to "...**measuring at least one function** modified by the binding..." While this language may be broad and require consideration under other statutes, it cannot be construed as 1) controlling the temperature (ie, as a parameter), and 2) measuring the temperature as an indication that your test compound has acted on the protein.

16. Rejection of Claims 4 under USC 112, 2nd paragraph for reciting expression of a form of G-protein without any clear relationship between it and the invention is maintained for reasons made of record in the action of 6/14/05 and 3/09/06 11/29/06. Applicant argues it is explained in section 19 of the specification and says the specification indicates that a chimeric g-protein which allows a modification of a signal path or introduction of a promiscuous g protein which binds readily. This would make sense if the transporter were g-protein linked. It is not clear how a g-protein relates to the instant transporter which is not a g-protein coupled receptor. See the arguments in prior office actions.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Rejection of claims 1, 10-12, 14 and 33 under 35 U.S.C. 102(b) as being anticipated by Jensen et al (1992) is maintained for reasons made of record in the action of 11/29/06 and reasons set forth below. Applicant argues that the 'functional parameters contemplated in the claime do not include the amount of the test substance administered or the physical behaviour of a test subject (page 10, Remarks). This is not found persuasive because Jensen et al demonstrate that the pain response measured is blocked by blocking NMDA receptors with MK-801. Thus, pain (which Jensen measures) is a measure of NMDA receptor activation. Applicant argues on page 11 of Remarks that "Jensen does not make clear that the glutamate was administered to one of the proteins, cells, or cell preparations cited in step (a). This is not found persuasive because Vglut1 is known to be present on neurons in the medulla (see below). Thus, Jensen et a inherently contacts cells expressing Vglut1 with glutamate and since Vglut1 is a glutamate transporter it necessarily flows from administration of glutamate to the medulla that the glutamate will contact Vglut1.

Applicant also notes that "Jensen states that administration of glutamate to a variety of brainstem sites elicited no response." This is not found persuasive because it is not relevant to the positive findings that sites that elicited a pain response were in the

medulla (see abstract, Jensen et al) and that vglut1 is present in ***pain ibers*** in the medulla (see Li et al, below). The failures are only relevant inasmuch as they indicate that Jensen et al had to stimulate grey matter that normally mediates a pain response to get the pain effect and that the pain effect was blocked by mk-801. The limitations of new claim 33 are met because Jensen et al test in an animal model of pain.

Conclusion

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Bellocchio et al show that glutamate binds to the Vglut1 transporter and is transported (see figure 1). Li et al show that Vglut1 is present in the medulla (see abstract).

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on **(571) 272-0841**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

/DAVID ROMEO/
PRIMARY EXAMINER
ART UNIT 1647

Steve Standley, Ph.D.
8/28/07